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REMARKS/ARGUMENTS

In the Claims

No claim amendments are presented with this Amendment.

In view of various comments regarding the present claims throughout prosecution of this application, Applicant notes for the record that pending claim 1 is limited to the three EAV ORFs indicated in the present claims (ORF 2, 5 and 7); the phrase "consisting of" is to show the vaccine does not include other EAV ORFs. Applicant also notes that the EAV ORFs may be present on the same nucleic acid or, preferably, on separate vectors, as evidenced for instance in pending claim 5 and in keeping with the Examples and discussion of the present application. This notation is meant for clarification purposes only, to avoid any potentially limiting interpretation of language of the Action on the present claims.

Response to Interview Summary issued by the Examiner on June 4, 2010

Applicant thanks the Examiner for taking the time and effort to detail her thoughts in the Interview Summary. Applicant respectfully notes for the record that while some aspects of the Interview and Interview Summary may be discussed herein, failure to discuss any aspect of the Examiner's Summary is not meant to indicate Applicant's assent to the remarks therewith.

Discussion

The present application has undergone 8 Office Actions since May 2006. During that time, rejections under 35 U.S.C. 102 and 103 based on a half dozen or more different documents have been made, considered, debated, and overcome, including rejections based on the presently cited Tobiasch document (rejections made in the Office Actions of July 14, 2006 and March 8, 2007 and withdrawn in the Office Action dated January 11, 2008). Rejections based on Tobiasch were newly raised in an Office Action dated October 16, 2008, in combination with yet another document, Snijder, under 35 U.S.C. 103. This was particularly disappointing to Applicant, as in that Action all previously pending rejections were overcome, and as no reason was given for creating the new rejection. Rejections based on Tobiasch in combination with Snijder are the sole rejections remaining in this application.

Applicants believe that the present invention is not obvious in view of Tobiasch and Snijder, and take this opportunity to attempt to persuade the Examiner of this, so as to avoid the rigors and expense of an Appeal.

The present invention is directed to a vaccine which is protective against equine arteritis virus (EAV) in horses and induces a cellular immune response, comprising a nucleic acid encoding an EAV sequence consisting of open reading frame (ORF) 2, ORF 5 and ORF 7. As indicated above, this claim is meant to restrict the present vaccine to only these three EAV ORFs; the present vaccine does not, for instance, include EAV ORF 4 or 6. The principle behind the vaccine is, once administered to a horse, to induce horse cells to make proteins encoded by these ORFs and stimulate the immune system. When EAV attempts to infect the horse, the immune system will be ready to protect the horse from infection.

This vaccine was the first of its kind, providing protection through both a sustained cellular and humoral immune response in horses vaccinated with the vaccine. The vaccine employs three ORFs never previously combined in this manner, in any in vitro or in vivo system, specifically selected and designed in view of research, expertise in the field, and plain old intuition. We discuss some of this research, expertise and intuition below, to show that the claimed invention would not have been obvious to the person skilled in the art in view of the facts of this case.

I. Equine Arteritis Virus (EAV), Tobiasch and the present invention

A. A few facts relating to Equine Arteritis Virus (EAV)

Infection by the Equine Arteritis Virus (EAV) can cause a variety of problems in horses. EAV has a fairly narrow range of infectivity, infecting only horses and donkeys. EAV has an RNA genome, 1-2% of which encodes several viral proteins via Open Reading Frames (ORFs) 1-7. The EAV genome is enclosed within a nucleocapsid made of protein "N" (encoded by ORF 7). The nucleocapsid is in turn enclosed within an envelope – a bilayer made of lipids and proteins -- that allows the virus to attach to and enter a host cell. ORFs 2-7 encode for "structural" EAV proteins, with ORF 2-6 proteins incorporated in or associated with the EAV envelope, and ORF 7 protein making up the nucleocapsid. See for instance the following summary of EAV ORF proteins and their characteristics:

- **ORFs 1a and 1b** encode for EAV replicase, translated directly from genomic RNA. ORFs 1a and 1b are located at the 5' end of the EAV genome, and are not believed to encode structural proteins.

- **ORF 2** encodes 2 minor structural membrane proteins:
  - Structural protein "E" (encoded by ORF 2a) - a 7-8 kDa, 67-residue polypeptide, largely hydrophobic with a central hydrophobic domain of 30-40 amino acids and a basic C-terminal domain. The protein is reported as indispensable for the generation of infectious virus particles, and as membrane-associated. E protein is unusual in that it migrates in gels as fuzzy doublet of between 6.5 and 10.5 kDa, even under reducing conditions. Snijder postulates that at least 2 forms of the protein may exist, and that post-translational modifications may affect how E protein associates with the EAV envelope.
  - Structural protein "Gs" (encoded by ORF 2b) – a 25 kDa protein also reported as needed for infectivity.

- As mentioned for instance at page 1 lines 33-34 of the present application, proteins encoded by **ORFs 3 and 4** were not well-characterized at the time of filing this application. However, ORF 4 was preliminarily reported to be a structural protein (see for instance Snijder page 6343 left column lines 23-25). Also, a homologous protein to ORF 4 – PRRSV ORF 4 – was known to be a secondary target for neutralizing antibodies in PRRSV. See for instance Snijder p. 6343 left column lines 21-23. Snijder left column page 6343 lines 19-31 reports some debate as to whether EAV ORF 3 is a structural or secretory protein, since homologous proteins in PRRSV and LDV were possibly secretory. As indicated in the Appendix, ORF 3 encodes a minor structural EAV protein.

- **ORF 5** encodes for structural protein "G_L" - 1 of 2 major EAV envelope proteins (30-44 kDa). G_L is the established EAV target for neutralizing antibodies.

- **ORF 6** encodes for structural protein "M" – the other major EAV envelope protein (16 - 17 kDa). M is a nonglycosylated, triple-spanning membrane protein.

- **ORF 7** encodes for structural protein "N" 14 kDa - the only nucleocapsid protein, ORF 7's protein N is considered 1 of 3 major structural EAV proteins, along with proteins encoded by ORFs 5 and 6 (structural proteins G_L and M, respectively). As discussed above, the nucleocapsid encases the EAV RNA genome and is covered by an envelope made of a lipid bilayer and structural proteins.

Overall, the 3 most 3'-proximal genes – ORFs 5, 6 and 7 – encode the three main structural components of the virus particle (respectively, proteins "G_L", "M" and "N"). Proteins considered to be minor structural components are encoded by ORF 2, ORF 3 and ORF 4.[1]

B. Tobiasch and the present invention

The inventors of the present invention are both authors of the "Tobiasch" document cited in the present Action. (Tobiasch et al., Virus Genes 22(2):187-199 (2001)). Tobiash discloses some preliminary research into the possibility of developing a DNA vaccine that protects against EAV infection in horses. The research included cloning Equine Arterivirus (EAV) Open Reading Frames (ORFs) 3, 4, 5 and 7 into vectors and introducing the vectors into Balb/c mice to express proteins encoded by the vectors. The mice were then monitored to see whether specific antibodies were made to the proteins. (Tobiasch Abstract lines 5-12 et al; page 193 right column).

Tobiasch reported successfully inducing immune response in mice with these vectors, stating in part that a significant immune response was detected when the animals were immunized with recombinant plasmids having ORF 7 or 5: the ORF7 plasmid induced an immune response in 80% of mice and 2 different ORF5 plasmids in 70 and 50% of mice, respectively. When expressed together, ORFs 5 and 7 produced an immune response in only 30% of mice. The best immune response was seen from the vector encoding only for ORF5 amino acids 1-121 (immune response detected in 90% of mice tested), known to represent the neutralizing portion of ORF 5. The worst results were from ORFs 3 and 4, which induced no (0%) immune response in any of the mice tested. See e.g. Tobiasch Table 2.

This research confirmed the vectors were able to be properly expressed and induce an antibody (humoral) immune response in mice. Mice are a convenient system for initial research, as they are inexpensive and easy to work with and the expression of proteins therein is well-documented. Tobiasch comments that the induction of immune response in these mice by ORFs 5 and 7 justified further research into the possibility of developing a model system to protect horses from EAV infection by cDNA vaccination. However, Tobiasch concludes, further studies in horse are required to assess the real protective potential of DNA vaccination in horse. (page 198 left column lines 23-26 and right column second full paragraph.)

[1] For further information on EAV structural proteins see for instance pages 1-2 of the present application; Tobiasch page 188 first paragraph left column; Snijder p. 6335, 2d paragraph; p. 6340 left column first full paragraph and right column lines 14-17; left column, p.6343 first full paragraph, ll.19-21; page 6344 left column top to middle.

As mentioned above, Tobiasch Table 2 indicated an attenuation of immune response in mice after co-administration of ORFs 5 and 7 (30%), as compared with ORFs 5 (70 and 50%) and 7 (80%). This data is reproduced in Table 5 of the present application and discussed in part at pages 32-34. Applicant performed further research on other EAV ORFs after publishing Tobiasch, and displayed the results of new research deemed most relevant to solving the present problem in Table 5 of the present application, entries 6 (ORF5+7+IL-2), 7(ORF5+6), 11 (ORF2+5+6+IL-2) and 12 (ORF2+4).

New Data in Table 5 of the present application

In further researching how to design the EAV vaccine of the present invention, Applicants considered whether the expression of IL-2 or ORF 6 vectors would enhance immune responses reported in Tobiasch.

i. ORFs 5, 7 and a vector encoding IL 2 were coadministered to see whether the presence of IL-2 would enhance the 30% immune response reported for the coadministration of ORFs 5 and 7 in Tobiasch. Enhanced EAV-specific immune response was seen when IL-2 vectors were coadministered with ORFs 5 and 7 (present application page 33 lines 27-28). The overall improvement in immune response was from 30% immune response (70% with neutralizing titer present) to 40% immune response (80% with neutralizing titer present). See Tobiasch Table 2 and the present Table 5 entries 5 and 6.

ii. ORFs 5 and 6 were coadministered to see whether the expression of major structural protein "M" from ORF 6 would enhance the 70% or 50% immune response reported from ORF 5 alone in Tobiasch. No EAV-specific enhancement of the immune response to ORF 5 was seen with ORF 6. Rather, an attenuation of immune response from 50 and 70% with ORF 5 alone to 20% with coadministration of ORF 5 and ORF 6 was seen. See page 33 line 30 to page 34 lines 6-8, and entries 3, 4 and 7 of Table 5 of the present application, as well as Tobiasch Table 2.

Applicants also coadministered ORFs 5 and 6 with ORF 2 and a vector to express IL-2, and report (Table 5 entry 11) an immune response in 70% of mice tested (90% with neutralizing titer, as indicated at page 35 lines 23-25). This is a substantial increase, in view of the 20% immune response (70% with neutralizing titer) reported with ORFs 5 and 6 alone, above. Overall, Applicant's new research shows that expression of ORF 5 alone induces an immune response in 50 or 70% of mice (Tobiasch), that coadministration of ORF5+6 induces an immune response in only 20% of mice tested (present Table 5 entry 7), and that coadministration of ORF5+6+2+IL-2 induces an immune response in 70% of animals (90% with neutralizing Titer; present Table 5 entry 11). Basically, the inclusion of ORF 2 as a 3d antigen source appeared to compensate for the attenuation of immune response seen when adding ORF 6 to ORF 5.

Applicants also considered the effect of ORF 2 on the 0% immune response reported from administration of ORF 4 in Tobiasch Table 2. As mentioned above, a homologous protein to ORF 4 – PRRSV ORF4 – was known to be a secondary target for neutralizing antibodies in PRRSV. The present Table 5 entry 12 and page 35 line 27 to page 36 line 4 of the application as filed report that coadministration of ORFs 2 and 4 resulted in 40% immune response (50% with neutralizing titer added).

Overall, this data showed that the inclusion of ORF 2 increased immune response in mice in up to 50% of mice (from 20% to 70%) when coadminstered with ORFs 5 and 6 and IL-2 (or from 70% to 90% with neutralizing titer added), and in up to 40% of mice, from 0% to 40% (or to 50% with neutralizing titer added), when coadministered with ORF 4.

While the data shown in Tobiasch Table 2 and in Table 5 of the present application show induction of an immune response (production of neutralizing antibodies), they do not and cannot show a protective response, because the studies occurred in mice. EAV has a limited host range, able to infect only horses (and donkeys) – not mice. At least for this reason, actual studies in horse were required to determine whether an effective, protective vaccine could be made to EAV.

Applicants considered this new data along with information available in the art, and selected ORFs 2, 5 and 7 as their best potential vaccine for experiments in horses. For instance, Appicants noted that the new ORF 2+5+6 data presented in Table 5 demonstrated no better effect than ORF 5 alone. ORF 5 and 6 are linked via a disulfide bridge in infectious and fully intact EAV. While such constructs can be useful in developing a vaccine, they may also complicate vaccine design and effectiveness. Based in part on the new data, the decision to leave major structrual protein ORF 6 out of the present vaccine was made.

As mentioned in paragraph 12 of Dr. Giese's Declaration filed April 2, 2009, other important considerations of the present invention included observations that the ORF 5 protein is a powerful immunogen but known for mutations, and data showing that ORF 7 and 2 provided, surprisingly, cytotoxic effects. For a successful fight against a virus, a complete immune response – humoral and cellular – is necessary. This selection occurred despite the knowledge that an internal protein such as ORF 7 would not typically be expected to provide cellular immunity, and that ORF 2 encodes a minor viral envelope protein that may provoke only minimal effects in recognizing EAV in vivo.

As the Examiner may be aware, the main purpose of a vaccine is to detect a virus when the virus is introduced into a host animal. If the virus does not display ORF 7 or ORF 2 on its envelope surface, the host immune system will have a difficult time recognizing the virus (relying on only the ORF 5 protein in a hopefully recognizable form). If the host immune system, whether humoral (antibody) or cellular (cytotoxic T-cells) does not become aware of the virus' presence, then the virus will be able to invade the host.

Examples 2 – 5 of the present application detail experiments devised to prepare a vaccine according to the present claims, including ORFs 2, 5 and 7, and to innoculate 5 horses of various ages with the vaccine. The vaccine was well-tolerated in all horses, and showed both a humoral (antibody) response and a specific cytotoxic response in all horses (see Tables 17, 19 and 20). As mentioned at paragraph 9 of Dr. Giese's April 2, 2009 Declaration, the induction of both a cellular and humoral immune response provides optimal protection against most virally caused infectious diseases. The present vaccine provided both of these, and successfully induced a stable and long-lasting immune response.

Tables 8 and 15 of the present application show the vaccination of horses with EAV ORFs 2, 5 and 7; Table 17 shows measurement of humoral (antibody) response in horses, and Tables 19 and 20 show the measure of specific lysis on an ORF-by-ORF basis for all horses. Overall, an increase of cell lysis at indicated times for each ORF was seen, compared to pre-immune values. This showed that ORFs 2, 5

and 7, coadminstered in horse, stimulated cellular immunity in an antigen-specific manner, and with the humoral immunity shown in Table 17, provided a protective vaccination for EAV.

II. Discussion of EAV, Tobiasch, the present invention and present Actions

Vaccine development is an unpredictable science. There's no recipe for the skilled person to follow, to know which if any viral protein or proteins will protect, which won't, which enhance or attenuate under what conditions; until they've been tested. As shown in Tobiasch, the fact that a structural EAV protein exists does not mean it will stimulate an immune response (ORFs 3, 4), and the fact that a protein is considered to be a major structural envelope protein does not mean it will enhance an immune response (ORF 6). The new data in Table 5 of the present application shows this with regard to ORFs 6 and 2: ORF 6 substantially decreased the immune response reported for ORF 5 alone (70/50% to 20% immune response), while ORF 2 (with IL-2) increased the immune response of coadministered ORFs 5 and 6 (20% to 70%), and of ORF 4 as well (0% to 40%).

Given the overall unpredictability of vaccines, and the lack of data relating to several EAV ORF proteins including ORFs 2a, 2b, 3, 4 and 6 at the time the present application was filed, Applicant respectfully submits that nothing in Tobiasch or Snijder teaches or could teach, alone or in combination, the present invention to the skilled person. For example, nothing in these documents would teach the skilled person that the 0% immune response seen with ORF 4 alone in Tobiasch could be increased to 40-50% when coadministered with ORF 2 (as shown in Table 5 of the present application), or that ORF 5+6 coadministered would attenuate immune response in mice and that attenuated response effectively restored with further coadministration with ORF2. Rather, Tobiasch does not measure immune response in mice by ORF2 at all, and Snijder simply reports on characteristics of the newly discovered ORF 2a "E" protein. Applicant respectfully submits that hindsight analysis based on the findings in the present application would be needed for the skilled person to combine Tobiasch and Snijder to find that EAV ORF 2 would be such a good enhancer of immune response, and ORF 6 not, that the skilled person would find the present invention obvious.

At least for the foregoing reasons, and in view of the demonstrated unpredictability in research geared toward creating a viable, protective EAV vaccine, Applicant respectfully submits that the present invention is not obvious in view of Tobiasch and Snijder, and requests withdrawal of the pending rejection to claim 1 and other claims therefore.

Other discussions relating to the pending obviousness rejections are as follows:

1. The skilled person would not be motivated to combine Tobiasch and Snijder in the manner indicated in the present Action.

Page 4 of the March 19, 2010 Action states the skilled person would be motivated to combine ORF 5 and 7 with ORF 2

> to induce a broad-range immune response against all arteriviral structural proteins, or to augment the immunogenic effect of ORF 5 and 7 with the one more structural antigen, ORF 2. One skilled in the art would be motivated to generate immune responses specific for a protein structure that better mimics the wild type EAV particle complete with all structural proteins. (Emphasis added).

Page 2 of the Advisory Action issued May 27, 2010 states the following reasoning for combining ORFs 2, 5 and 7:

> the combination of the ORF2, ORF5 and ORF7 into one expression vector for cDNA vaccination, which is for the purpose of generating a broad spectrum multi-antigenic immune response against all the EAV structural proteins, which are ORF2, ORF5, and ORF7, rather than eliciting immune response against only one of them. (Emphasis added).

In reviewing these passages, and others issued throughout prosecution of this application, Applicant recognized that a miscommunication has occurred with regard to the nature of the EAV ORF proteins. The present rejection appears to have been maintained against the present invention, which is restricted to EAV ORFs 2, 5 and 7 and no other EAV ORFs, in view of the patent office's statements that ORFs 2, 5 and 7 consist of all of the EAV structural proteins. This miscommunication would explain a great deal of the Examiner's position to the undersigned representative, as it would clarify why the present rejections maintain that Tobiasch and Snijder together taught a vaccine having 3 and only 3 EAV ORFs when there are 7 structural ORF EAV proteins to choose from.

Applicant respectfully notes that all proteins made from EAV ORF 2, 3, 4, 5, 6 and 7 are structural proteins. See section I.A. above, discussing 7 known structural proteins of EAV. The present invention is limited to a vaccine having only EAV ORFs 2, 5 and 7, selected by the inventors of this invention in view of years of expertise, research, and intuition, as discussed in section I.B. above.

In response to the present obviousness rejection, Applicant respectfully submits that the skilled person would not be motivated to combine the ORF 5+7 discussed in Tobiasch in view of Snijder's disclosure of the discovery of the "E" protein encoded by ORF 2a, or other disclosures relating to ORF 2. ORF 2 is not the third and only remaining structural protein encoded by the EAV ORF genome, after ORF 5 and 7. Rather, the skilled person would be aware of structural proteins encoded by ORFs 2a and b, 3, 4 and 6 (with some question at the time of filing as to whether ORF 3 encoded for a structural or secretory protein). Applicant respectfully submits the motivation indicated in the Action, to include all structural EAV proteins, does not apply to the present invention in view of the existence of 7 structural EAV proteins, and requests withdrawal of the pending 103 rejections therefore. Furthermore, as there are 7 structural EAV proteins, it would appear that the teaching set forth in the present Action is that all 7 proteins should be in the vaccine, to ensure breadth the nearest wild type virus. Applicant respectfully submits that the present vaccine's achievement of full protection with only 3 viral components is not obvious therefore.

As the present invention is not directed to all of EAV ORFs 2-7 and their commensurate structural proteins, but rather only to a select number of EAV ORFs, Applicant respectfully submits that motivation indicated at page 4 of the Action does not apply to the present invention, that no motivation exists to select specifically 3 EAV proteins out of the 7 possible, and that the present invention is not obvious therefore.

Furthermore, Applicant respectfully submits that the skilled person would not be motivated to combine Tobiasch's disclosure of ORFs 5 and 7 with Snijder's disclosure of ORF 2 to prepare the present invention at least because the nucleocapsid protein (encoded by ORF 7) in the present vaccine would be expected to be situated internally within the virus. Tobiasch reports that the ORF 7 vector was able to generate an immune response in mice, however, recognition by cytotoxic T-cells in horses as seen in Tables 19-20 of the present application was unexpected because the T-cells wouldn't be expected to

detect the EAV ORF 7 protein upon viral infection, if the protein is hidden under the virus' envelope lipids and proteins. See for instance inventor Giese's Declaration, paragraph 14, submitted April 2, 2009 in this application, wherein Dr. Giese theorizes that mobilization of the T-cell response to the ORF 7 antigen may be due to imperfect translation of mRNA to protein during the viral replication process, which causes mistakes in the nucleocapsid protein assembly and thereby provokes this immune response.

Furthermore, Applicant respectfully submits that the skilled person would not be motivated to combine Tobiasch's disclosure of ORFs 5 and 7 with Snijder's disclosure of ORF 2 at least because, as discussed above, the skilled person would not be taught that ORF 2 would so greatly increase immune response in mice when coadministered with ORF 5, 6 and an IL-2 vector (20% to 70%, without neutralizing titer included) or with ORF 4 (0% to 40%, without neutralizing titer). (See Section I.B. and first paragraph of Section II, above). Also, see the below discussion of ORF 2 as discussed in paragraph 12 of Dr. Giese's above April 2, 2009 Declaration:

> The naturally low EAV ORF 2 antigen concentration was thought by scientists in this field to contribute to the extremely poor antigenic recognition of ORF 2 protein, i.e. limited antibody response, that was observed in one mouse B-cell model (Chirnside, of record). This observation may explain why, until now, the use of ORF 2 with other ORFs in a vaccine composition has not been pursued. This, in part, explains our statement in [0057] in the Application where we note that it was "surprising" and "contrary to the opinion in the art" that our vaccine composition comprising the three above-mentioned ORFs provided improved, and longer lasting, sustainable results than studies using the entire EAV cDNA sequence (e.g. Chirnside). However, the data presented in Table 17 clearly show a sustained immune response following a vaccination with our EAV vaccine compositions (humoral response), while Tables 19-20 show an elevated and sustained (cellular) response at the indicated points in time.

2. The attenuated immune response reported by Tobiasch for ORF 5+7 teaches the skilled person away from the ORF 2+5+7 vaccine of the present invention.

As previously submitted to the Examiner, taken as a whole, Tobiasch teaches away from the present invention by disclosing that the coadministration of ORF 5 and 7 in mice dramatically decreased immune response from 80% (ORF 7 alone) and 70% or 50% (ORF 5 alone) to 30% (ORF 7 and ORF 5 coadministered; Tobiasch Table 2). Applicant requests that the Examiner reconsider these arguments, presented in the previous response filed in this application, in view of the above discussion advising that the EAV ORF genome encodes for more than 3 structural proteins.

Applicant notes that comparative data does not exist for ORF 5 alone and ORF 7 alone in Tobiasch Table 2, and that for this reason the Applicant cannot phrase this argument in terms of data where neutralizing titer is included, despite every wish to accommodate the Examiner. The Examiner's indication in the second paragraph of the June 4 Interview Summary, comparing data including neutralizing titer from the truncated version of ORF 5 (100% immune response; Entry 8, Tobiasch Table 2) with data including neutralizing titer from the coadminstration of ORFs 5 and 7 (70% immune response; Entry 5, Tobiasch Table 2), is problematic in that the ORF 5s being compared are substantially different (whole vs. truncated).

In the May 27, 2010 Advisory Action, the Examiner states in part that

> Applicant's assertion that the ORF5+7 vaccine is inferior to either ORF5 or ORF7 alone is solely based on the % of immune response detected but not on any actual EAV protection/challenge study results. It is known in the art that a higher amount of immune response raised against a single viral antigen cannot be equated to a more protective vaccine.

This is reiterated in paragraph 3 of the June 4 Interview Summary issued by the Examiner.

Applicant agrees that the results set forth in Tobiasch will not necessarily predict that which will be protective in a horse. Applicant also respectfully notes that it would be unfair to base the present rejection under 35 U.S.C. 103 on Tobiasch's coadministration of ORFs 5 and 7 in mice, and then hold data related to that coadministration of ORFs 5 and 7 as irrelevant because it occurred in mice.

The interpretation of the data as both meaningful (qualitative antibody response either present or not) and meaningless (quantitative 70% vs. 30% difference discounted as not translating to horses), if maintained, unfairly takes those parts of Tobiasch that support the present 103 rejection and ignores the rest. The skilled person in the art may well find meaning in those numbers, taking Tobiasch as a whole, particularly as the data is clearly presented in quatitative fashion in Tobiasch Table 2.

3. Tobiasch does not teach a vaccine that protects against EAV infection and induces a cellular response in horses.

Page 3 of the present Action states that Tobiasch teaches prevention of EAV in horses by DNA vaccination, with a vaccine composition comprising one or several vectors having ORF 3, 4, 5 or 7. The Action further notes that the vaccine composition of Tobiasch further comprises PBS, characterizing such as a pharmaceutically acceptable carrier or excipient.

As the Examiner may recall, all data from Tobiasch is in mice. Mice are not within the host range of EAV; EAV infects only horses (and perhaps donkeys). Applicant respectfully points out page 7 lines 27-32 of the application as filed, indicating that the EAV vaccine according to the invention confers active immunity against a disease provoked by EAV. No protective benefit would be seen from the introduction of the ORFs disclosed e.g. in Tobiasch Table 2 into mice. Rather, the EAV ORFs were introduced only to determine whether the ORF vectors could express their respective proteins and whether the proteins would stimulate a humoral (antibody) immune response in mice. Applicant respectfully submits, therefore, that Tobiasch does not teach a vaccine that is protective in horses, at least because no indication of protection is made throughout the document.

Page 9 of the March 19 Action states, with regard to Applicant's previously submitted argument that Tobiasch's disclosure does not translate to a vaccine protective against EAV infections in horses, that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

In response, Applicant respectfully notes that, as indicated in the present Action, the vaccine of the present invention provides a protective response in horses, and is structurally different (ORFs 2, 5, 7) from Tobiasch's compositions (ORFs 5+7). Applicant respectfully submits that Tobiasch's disclosure does not translate to a vaccine protective against EAV infections in horses, according to Applicant's knowledge set forth in the present application, because Tobiasch uses only mice; mice are not EAV hosts

and do not need protection from EAV; and Tobiasch's compositions are structurally different from the present claims.

Page 9 of the Action states that the recitation protective against EAV infections in horses has not been given patentable weight because the recitation occurs in the preamble, and that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone.

In response, Applicant respectfully notes that the preamble of claim 1 is directed in part to an EAV vaccine that is protective in horses. In response, Applicant respectfully submits that the preamble of claim 1 does not merely recite the purpose of a process or intended use of a structure, but rather is tied to the EAV ORF structures set forth in the body of the claim (for instance because EAV can only infect horses (and possibly donkeys), and the ORFs disclosed in the body of claim 1 are expressly and only EAV ORFs.).

In the event that the Examiner believes that moving any aspect of the preamble into the body of the claim will facilitate allowance of this application, the Examiner is invited to contact the below representative by telephone to discuss.

At least in view of the foregoing discussion, Applicant respectfully submits that all pending rejections under 35 U.S.C. 103 are overcome, and requests that the Examiner withdraw the pending rejections and allow this application to proceed to grant.

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Applicant respectfully requests allowance of the above-identified application. In the event that the Examiner has any questions or concerns regarding this Amendment, or any further concerns regarding allowing this application, the Examiner is invited to contact the below-signed representative by telephone to discuss.

Respectfully submitted,

August 19, 2010
Date

Valerie Neymeyer-Tynkov
Reg. No. 46,956
Neymeyer-Tynkov LLC
20 N. Clark St. Suite 600
Chicago, IL 60602
Phone: 312/965-1969

APPENDIX

Journal List > J Virol > v.76(21); Nov 2002

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Characterization of Two New Structural Glycoproteins, GP_3 and GP_4, of Equine Arteritis Virus

Roeland Wieringa,* Antoine A. F. de Vries,† Martin J. B. Raamsman,‡ and Peter J. M. Rottier

Virology Division, Department of Infectious Diseases and Immunology, Faculty of Veterinary Medicine, and Institute of Biomembranes, Utrecht University, 3584 CL Utrecht, The Netherlands
*Corresponding author. Mailing address: Virology Division, Department of Infectious Diseases and Immunology, Yalelaan 1, 3584 CL Utrecht, The Netherlands. Phone: 31-30-2532468. Fax: 31-30-2536723. E-mail: r.wieringa@vet.uu.nl.
†Present address: Gene Therapy Section, Department of Molecular Cell Biology, Leiden University Medical Center (LUMC), 2333 AL Leiden, The Netherlands.
‡Present address: Crucell N.V., 2333 CN Leiden, The Netherlands.

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ABSTRACT

Equine arteritis virus (EAV) is an enveloped, positive-stranded RNA virus belonging to the family *Arteriviridae* of the order *Nidovirales*. Four envelope proteins have hitherto been identified in EAV particles: the predominant membrane proteins M and G_L, the unglycosylated small envelope protein E, and the nonabundant membrane glycoprotein G_S. In this study, we established that the products of EAV open reading frame 3 (ORF3) and ORF4 (designated GP_3 and GP_4, respectively) are also minor structural glycoproteins. The proteins were first characterized by various analyses after in vitro translation of RNA transcripts in a rabbit reticulocyte lysate in the presence and absence of microsomal membranes. We subsequently expressed ORF3 and -4 in baby hamster kidney cells by using the vaccinia virus expression system and, finally, analyzed the GP_3 and GP_4 proteins synthesized in EAV infected cells. The results showed that GP_4 is a class I integral membrane protein of 28 kDa with three functional N-glycosylation sites and with little, if any, of its carboxy terminus exposed. Both after independent expression and in EAV-infected cells, the protein localizes in the endoplasmic reticulum (ER), as demonstrated biochemically by analysis of its oligosaccharide side chains and as visualized directly by immunofluorescence studies. GP_3, on the other hand, is a heavily glycosylated protein whose hydrophobic amino terminus is not cleaved off. It is an integral membrane protein anchored by either or both of its hydrophobic terminal domains and with no parts detectably exposed cytoplasmically. Also, GP_3 localizes in the ER when expressed independently and in the context of an EAV infection. Only a small fraction of the GP_3 and GP_4 proteins synthesized in infected cells ends up in virions. Most, but not all, of the oligosaccharides of these virion glycoproteins are biochemically mature. Our results bring the number of EAV envelope proteins to six.

Equine arteritis virus (EAV), the etiological agent of equine viral arteritis (9, 11, 45), has been assigned to the family *Arteriviridae*. The *Arteriviridae* constitute the single genus *Arterivirus*. Other members of this genus are lactate dehydrogenase-elevating virus (LDV), porcine reproductive and respiratory syndrome virus (PRRSV), and simian hemorrhagic fever virus (SHFV). Although